

Figure 1. Event free survival in children belonging to upper, middle and lower socioeconomic (SE) strata, after excluding patients who died in induction.

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DOES DISTANCE BETWEEN RESIDENCE AND TREATING CENTER IMPACT OUTCOME IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA? REPORT FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Background: Patients in our country often live far from the oncology center. Amongst the numerous socio-demographic factors which affect outcome, it is postulated that outcome may have a relationship to the proximity of the patient to the tertiary care center.

Aim: To study if distance between home and the treating center influenced outcome in childhood acute lymphoblastic leukemia (ALL).

Methods: A retrospective analysis of children diagnosed and treated for ALL from January 2010 to December 2012 were included. Patients were treated as per modified UKALL-2003 protocol. Details of residential address were noted from the database maintained by the social worker. Patients were instructed to stay within an hour's distance of hospital till the completion of delayed intensification phase of therapy. During maintenance therapy, they visit the oncology center monthly from their place of residence. Distance between Chandigarh and district of residence of the patient was recorded. Patients were classified based on this distance in kilometers (km) into 3 groups; group 1: 0-50 km, 2: 50-200 km, 3: > 200 km. Induction failure, death and relapse were included as events for Kaplan-Meier survival analysis.

Results: The study included 308 patients with median age of 5 years (range: 1-13). Male to female ratio was 2.5:1. Numbers of patients hailing from rural and urban areas were 198 (64%) and 110 (36%). Sixty-five (21%), 133 (43%) and 110 (36%) patients belonged to groups 1, 2 and 3. Sixteen patients abandoned treatment. The incidence of abandonment did not differ significantly between the 3 groups ($p=0.305$). Neutropenic deaths occurred in 19 patients during maintenance therapy. However, maintenance deaths were similar among the 3 groups ($p=0.409$). Event-free-survival (EFS) in groups 1, 2 and 3 was not different: $63.7 \pm 6.6\%$, $57.8 \pm 4.6\%$ and $55.1 \pm 5.4\%$ ($p=0.557$, Fig. 1). Overall-survival (OS) did not differ between groups 1, 2 and 3: $76.4 \pm 6.2\%$, $75.3 \pm 3.8\%$ and $73.4 \pm 4.6\%$ ($p=0.810$). EFS and OS did not differ between rural and urban patients ($54.5 \pm 3.9\%$ vs. $64.6 \pm 5\%$, $p=0.166$; $73.6 \pm 3.3\%$ vs. $76.6 \pm 4.7\%$, $p=0.524$).

Conclusions: Distance between patients' residence and the treating center does not impact survival in childhood ALL. Patients hailing from rural and urban backgrounds do not differ in their survival.

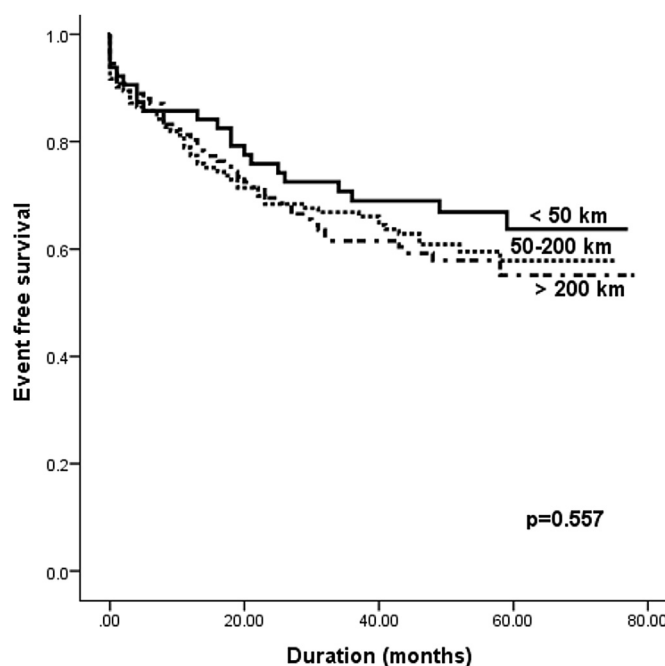


Figure 1. Event free survival of patients belonging to areas < 50 km, 50-200 km and > 200 km from treating center (Chandigarh).

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PROFILE OF INFECTIONS DURING INDUCTION CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Infections are a major cause of mortality and morbidity in pediatric ALL patients especially during induction chemotherapy. We present the profile of infections among 227 consecutive patients who presented with ALL during an 18-month period. Information on the clinical and microbiological profile of infections is very important in the counseling, management and prognostication of patients with ALL.

Objective: To describe the clinical and microbiological profile, treatment and outcome of infections during induction chemotherapy in children with ALL.

Method: This was a prospective observational study. All children (Age: 1 – 14 years) newly diagnosed to have ALL and seeking the services of the Pediatric oncology division at our Center during the study period were included. Induction chemotherapy was administered as per a modified BFM protocol, for all.

Observations: 227 patients (144 belonged to high risk category and 83 belonged to standard risk category) were enrolled during the study period (January 2014 to June 2015). There were 150 episodes of infection which occurred among 117 patients. Major sites were lung ($n=35$) and GIT ($n=30$). No definite focus of infection was evident in 28%. Blood cultures were positive in 45 episodes (30.6%). Isolates were gram negative organisms ($n=36$; 80%) in the majority in whom culture was positive. Five of the isolates were fungal out of which two were in combination with *Pseudomonas*. 127 episodes were initially treated with first line antibiotics, 19 episodes with second line antibiotics and 4 episodes with third line antibiotics based upon the severity of infection. Eventually, 127 episodes received first line, 47 episodes received second line and 28 episodes received third line antibiotics as per institutional protocol. Antifungals were given in 29 episodes (19.3%). 24 among them were empirical and the rest based on positive culture reports. Intensive supportive care in the form of inotropes or mechanical ventilation was required in 17 episodes (11.3%). One hundred and thirty six (90.6%) episodes resolved without sequelae. Twelve patients (8%) died (One of them had varicella with hepatitis and

coagulopathy) and two patients survived with sequelae. Overall induction mortality (12 out of 227 - 5.3%) was solely accounted for by infections. Hemodynamic instability and tachypnoea were the only predictors of mortality, which was independent of laboratory parameters or culture positivity.

Conclusions: Infections were a major cause of morbidity and the sole cause of mortality in pediatric ALL during induction chemotherapy, in our series. Around half of the patients had at least one episode of infection; gram negative organisms are the predominant isolates in blood culture. Most infections respond well to standard antibiotic regimens and sequelae in survivors are rare.

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ETIOLOGICAL PROFILE OF SEIZURES IN CHILDREN UNDERGOING CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: The prevalence of seizures in the ALL population is reported to vary between 8 and 13%. Not much is known about the etiology, natural history of these seizure, the risk factors for their recurrence, and the long-term need for antiepileptic drug (AED) treatment. Also little is known about the risk of interaction of AED with chemotherapeutic agents, hence the dose modifications needed in chemotherapy when on chronic AEDs. A data regarding the same from Indian population is lacking.

Methods: It was a Prospective descriptive study, conducted at Pediatric oncology division of Regional Cancer Centre, Thiruvananthapuram. All children between the age of 0-14 years, with no pre-existing neurological abnormality developing first episode of seizure during the period of ALL chemotherapy were included. All relevant clinical, treatment related and investigational data were collected prospectively and analyzed.

Results: 28 patients (7.84%) developed seizures out of 357 patients with ALL during the study period. Majority of seizures occurred in the B-ALL immunophenotype, HR groups, during induction chemotherapy. 24 patients (85.7%) presented with generalized seizure with 13 patients (46.4%) having status epilepticus. The etiological factors identified included (in decreasing order of frequency) CVT, meningitis, encephalitis, febrile seizures, SIADH, hypertension, hypoxia, PRES, Mineralizing microangiopathy, Sepsis, Gliosis, ADEM, CNS leukemia. 16 patients (57.1%) had associated hyponatremia. CT scan detected cortical venous thrombosis (CVT) in 5 patients (17.8%). Recurrence of seizure [occurred in 12 patients (42.9%)] was the only factor that reached statistical significance when need for antiepileptic drug prophylaxis was assessed.

Conclusion: Data regarding incidence and etiology of seizures in ALL is lacking and majority of studies attribute chemotherapy and / or radiotherapy as the cause when a definitive etiology could not be found. An etiology could be detected in 92.8% of seizure episodes in our study with majority being treatment related complication or related to infections. Most of the episodes occur during induction chemotherapy probably reflecting the intensity of treatment and active disease in the patient. HD MTX was given in a quarter of children with seizure during ALL chemotherapy, but typical imaging finding suggestive of CNS involvement by methotrexate was rare. Multiple electrolyte abnormalities were a common finding, stressing the need for monitoring of electrolytes and keeping them in the normal range during ALL chemotherapy, to keep neurological morbidity to the minimum. AED prophylaxis was needed in two thirds of patients, with recurrence of seizure being the most important predictor for requirement of prophylaxis. Permanent neurological deficit was present in one fifth of children with seizure, suggesting the need for a multidisciplinary approach.

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CYTOGENETICS IN B CELL ALL

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Introduction: Chromosomal abnormalities are hallmark of lymphoblastic leukemia. Cytogenetic studies have identified numerical and structural chromosomal abnormalities which have fundamental importance in the diagnosis, risk stratification, monitoring post-transplant bone marrow and to assign prognosis.

Aim: To report common cytogenetic abnormalities in B cell ALL patients at our centre.

Methods: Patients of ALL below 18 years of age, since December 2013 were enrolled and treated on ICicle protocols. G-banding or FISH was done for common cytogenetic abnormalities such as t(12;21), t(4;11), t(9;22) & t(1;19).

Results: Over the period of 33 months, 119 cases of ALL (B cell 99, T cell 20) were started on treatment. Records of 99 patients of B cell ALL were reviewed for cytogenetics. M:F ratio was 2.41:1. Eighty five (85.85%) were between 1-10 year and 14 (14.14%) were above 10 year. Sixteen (16.16%) were assigned as SR, 65 (65.65%) as IR and 18 (18.18%) as HR. Thirty nine (39.39%) patients had cytogenetic abnormalities.

Twelve (12.12%) were t(9;22), 18 (18.18%) were t(12;21), 7(7.07%) were t(1;19) positive respectively. None were t(4;11) positive. Two patient had hyperploidy and one had del (1)(q25). t(12;21) and t(1;19) had male preponderance. Among patients with t(9;22), 58.33% were above 10 years and 58.33% had hyperleukocytosis. All patients with t(1;19) & two with t(12;21) were assigned as IR & HR respectively.

Conclusion: Translocation t(12;21) was the commonest abnormality. Frequency of t(9;22) BCR-ABL was higher while frequency of hyperploidy was lower to that described in western literature.

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AVOIDING CRANIAL RADIOTHERAPY FOR MOST CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE CENTER STUDY OF CNS OUTCOME

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Background/objective: CNS relapse occurs in 3-8% of children treated for acute lymphoblastic leukemia (ALL) and poses a major obstacle in the long-term cure. Prophylactic cranial radiotherapy (pCRT) and intrathecal chemotherapy (IT) are both known to prevent this complication. pCRT is increasingly being avoided in this cohort in view of the known late effects associated with this modality. However, a number of centers continue to use it for T cell disease and high risk patients. We hereby report the experience of our center in terms of CNS control of leukemia by using the strategy of IT alone and a conservative approach of using pCRT.

Methods: We conducted a retrospective chart review of children with ALL from age 1- 18 years who took treatment in our unit from October 2002 to August 2016. The children were treated as per COG protocol which comprised of dexamethasone in induction for children less than 10 years of age. High dose methotrexate at 5 gm/m² for high risk (HR) ALL and at 3 gm/m² for standard risk (SR) ALL was included in the treatment regimen from 2009 onwards. A total of 20- 22 doses of IT were given. Children with CNS leukemia at diagnosis received 18 Gy of CRT and triple IT and others received only intrathecal methotrexate. T cell immunophenotype was not a criterion for giving pCRT. Standard protocols for sedation and positioning were strictly adhered to during IT administration with the first IT being performed only by a consultant.

Results: Study population comprised of 250 consecutive children with ALL (70.4% were males) with a median age of 7.19 +/- 4.70 years (Range 1- 18 years). The median follow up was 1575 +/- 1424.7 days (Range 6- 5147 days). Patients less than 1 year of age at diagnosis, and those who continued treatment at another center have been excluded from this analysis. SR ALL was seen in 126 children (50.4%), 110 had HR (44%) and 14 had very high risk (VHR) disease (5.6%). B-lineage ALL was present in 210 children (84%), 37 had T-lineage ALL (14.8%) and 3 had biphenotypic ALL (1.2%). Five children had CNS leukemia at diagnosis. pCRT was given to 11 children (4.4%) which included the above 5, 1 with VHR ALL, and an additional 5 for concerns regarding inability to travel for regular IT during maintenance. Six children eventually had a CNS relapse (2.4%), 3 of these had already received pCRT. One other patient had an orbital relapse of leukemia and 2 had a combined bone marrow and CNS relapse. Only 2